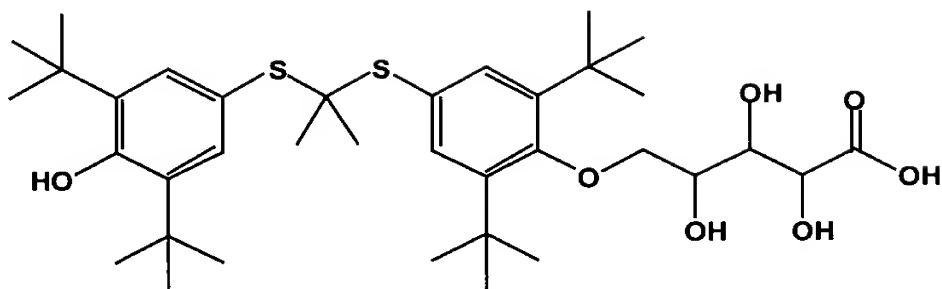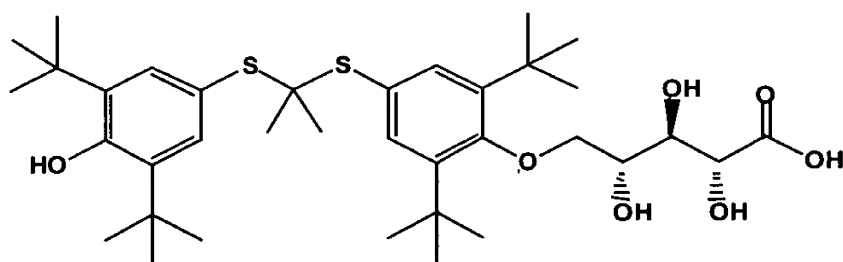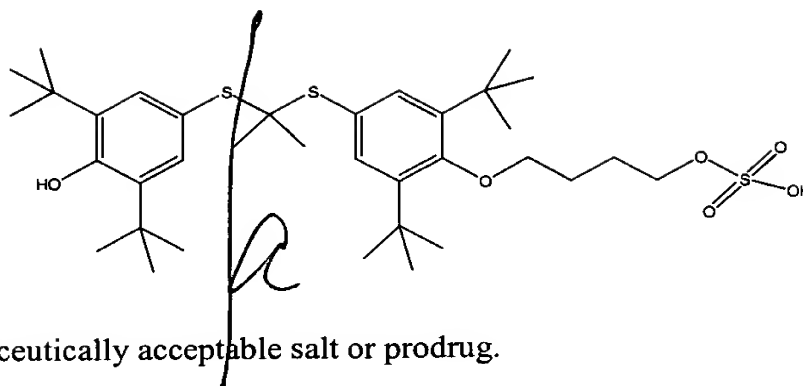We claim

1.   A compound of the formula:

or its pharmaceutically acceptable salt or prodrug.

2.   A compound of claim 1 of the formula:

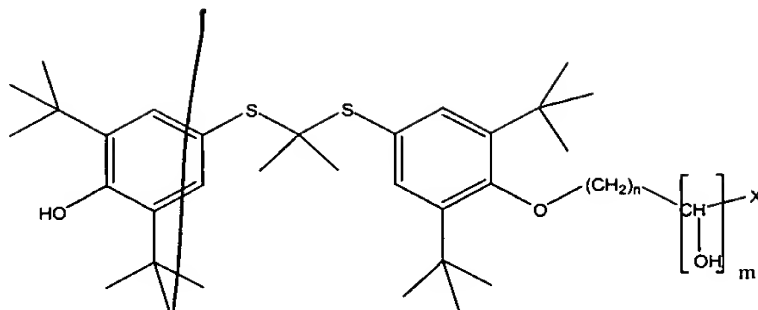or its pharmaceutically acceptable salt or prodrug.
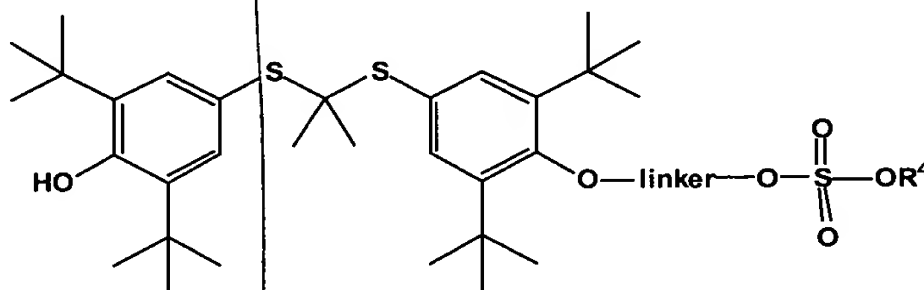
3.   The compound of the formula:

or its pharmaceutically acceptable salt or prodrug.

4. A method for increasing high density lipoprotein cholesterol level in a host comprising administering an effective amount of the compound of claim 1.

5. A method to improve the functionality of circulating high density lipoprotein in a host, comprising administering an effective amount of the compound of claim 1.

6. A method for increasing high density lipoprotein cholesterol level in a host comprising administering an effective amount of the compound of claim 2

7. A method to improve the functionality of circulating high density lipoprotein in a host, comprising administering an effective amount of the compound of claim 2.

8. A method for increasing high density lipoprotein cholesterol level in a host comprising administering an effective amount of the compound of claim 3.

9. A method to improve the functionality of circulating high density lipoprotein in a host, comprising administering an effective amount of the compound of claim 3.

10. A compound of the formula:

wherein

X= $CH_2C(O)_2R$, $C(O)_2R$, or $C(O)NR^1R^2$; n= 1, 2, 3, 4, or 5; m= 2, 3, 4, 5, 6, or 7; and

R, R^1 and R^2 are independently hydrogen, alkyl, aryl, aralkyl, or alkaryl, which can be

optionally substituted; or its pharmaceutically acceptable salt or prodrug.

11.   The compound of claim 10, wherein X is $C(O)_2R$.

12.   The compound of claim 10, wherein n is 1, 2, or 3.

13.   The compound of claim 10, wherein m is 3, 4, 5, or 6.
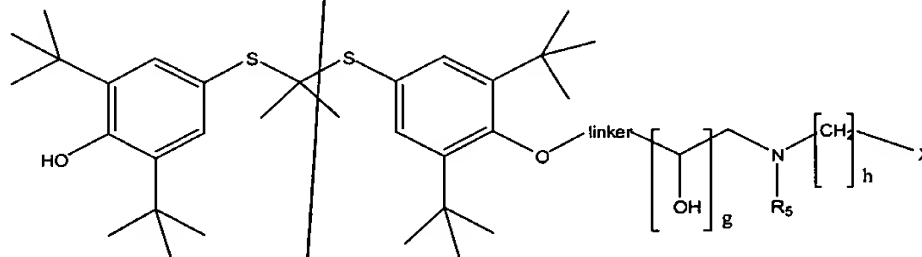
14.   A compound of the formula

wherein

linker is alkyl or lower alkyl, alkenyl, alkynyl, heterocyclic, heteroaryl, aryl, aralkyl,

heterocyclicalkyl, heteroarylalkyl, alkaryl, alkylheterocyclic, or alkylheteroaryl, which can be

optionally substituted and R^4 is hydrogen, alkyl, alkenyl, alkynyl, heterocyclic, heteroaryl, aryl,

aralkyl, heterocyclicalkyl, heteroarylalkyl, alkaryl, alkylheterocyclic, or alkylheteroaryl which

can be optionally substituted; or its pharmaceutically acceptable salt or prodrug.

15.   The compound of claim 14, wherein the linker is $-(CH_2)_k-$ and k is 2, 3, 4, 5, 6, 7, 8, 9,

or 10.

16.   The compound of claim 14, wherein k is 3, 4, 5, or 6.

17.   The compound of claim 14, wherein R^4 is hydrogen.

18.   A method for increasing high density lipoprotein cholesterol level in a host comprising

administering an effective amount of a compound of the formula:

X= CH$_2$C(O)$_2$R, C(O)$_2$R, or C(O)NR^{1}R^2; h= 1, 2, or 3; g= 1, 2, 3, 4, 5, 6, or 7; and R,

R^1, R^2 and R^5 are independently hydrogen, alkyl, aryl, aralkyl, or alkaryl, which can be

optionally substituted; linker is alkyl or lower alkyl; or its pharmaceutically acceptable salt or

prodrug.

19.   The method of claim 18, wherein X is COOR.

20.   The method of claim 18, wherein X is COOH.

21.   The method of claim 18, wherein R^5 is hydrogen.

22.   The method of claim 18, wherein the linker is -(CH$_2$)$_j$- and j is 1, 2, or 3.

23.   The method of claim 18, wherein the linker is -(CH$_2$)$_j$- and j is 1.

24.   The method of claim 23, wherein h is 1.

25.   The method of claim 23, wherein g is 1.

26.   The method of claim 21, wherein the compound is in the form of a pharmaceutically

acceptable salt.

27.   A method for increasing high density lipoprotein cholesterol level in a host comprising

administering an effective amount of a compound of the formula:

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wherein

X= $CH_2C(O)_2R$, $C(O)_2R$, or $C(O)NR^1R^2$; n= 1, 2, 3, 4, or 5; m= 2, 3, 4, 5, 6, or 7; and

R, R^1 and R^2 are independently hydrogen, alkyl, aryl, aralkyl, or alkaryl, which can be optionally substituted; or its pharmaceutically acceptable salt or prodrug.

28.   The method of claim 27, wherein X is $C(O)_2R$.

29.   The method of claim 27, wherein n is 1, 2, or 3.

30.   The method of claim 27, wherein m is 3, 4, 5, or 6.

31.   A method for increasing high density lipoprotein cholesterol level in a host comprising administering an effective amount of a compound of the formula
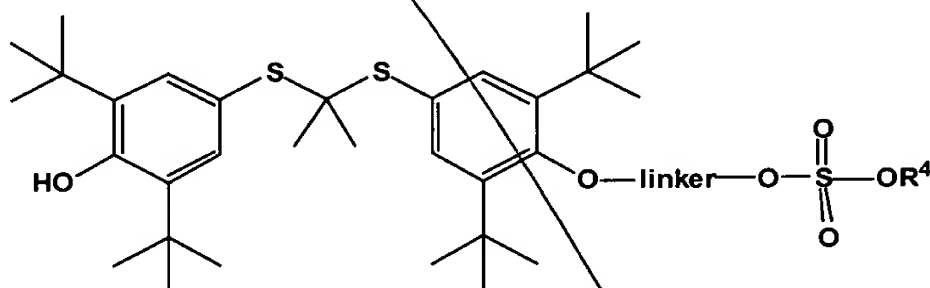

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wherein

linker is alkyl or lower alkyl, alkenyl, alkynyl, heterocyclic, heteroaryl, aryl, aralkyl, heterocyclicalkyl, heteroarylalkyl, alkaryl, alkylheterocyclic, or alkylheteroaryl, which can be optionally substituted and R^4 is hydrogen, alkyl, alkenyl, alkynyl, heterocyclic, heteroaryl, aryl, aralkyl, heterocyclicalkyl, heteroarylalkyl, alkaryl, alkylheterocyclic, or alkylheteroaryl which can be optionally substituted; or its pharmaceutically acceptable salt or prodrug.

32.   The method of claim 31, wherein the linker is -(CH$_2$)$_k$- and k is 2, 3, 4, 5, 6, 7, 8, 9, or 10.

33.   The method of claim 31, wherein k is 3, 4, 5, or 6.

34.   The method of claim 31, wherein R^4 is hydrogen.

35.   A pharmaceutical composition for increasing plasma HDLc or improving HDL functionality in a subject comprising an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt or prodrug thereof, and a pharmaceutically acceptable carrier.

36.   A pharmaceutical composition for increasing plasma HDLc or improving HDL functionality in a subject comprising an effective amount of a compound of claim 2 or a pharmaceutically acceptable salt or prodrug thereof, and a pharmaceutically acceptable carrier.

37.   A pharmaceutical composition for increasing plasma HDLc or improving HDL functionality in a subject comprising an effective amount of a compound of claim 3 or a pharmaceutically acceptable salt or prodrug thereof, and a pharmaceutically acceptable carrier.

38.   A pharmaceutical composition for increasing plasma HDLc or improving HDL functionality in a subject comprising an effective amount of a compound of claim 10 or a pharmaceutically acceptable salt or prodrug thereof, and a pharmaceutically acceptable carrier.

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39.　A pharmaceutical composition for increasing plasma HDLc or improving HDL functionality in a subject comprising an effective amount of a compound of claim 14 or a pharmaceutically acceptable salt or prodrug thereof, and a pharmaceutically acceptable carrier.

40.　A method of determining whether a compound effectively increases HDLc *in vivo* and improves HDL functionality *in vivo* or *in vitro* comprising:

　　a)　contacting the compound with cholesterol-containing HDL,

　　b)　determining whether the compound and cholesterol-containing HDL form a complex,

　　c)　determining whether the compound increases the half life of apoAI-HDL, and

　　d)　determining whether the compound increases the selective uptake of cholesterol or cholesteryl esters by hepatic cells.

41.　The method of claim 40 wherein the increase in half life of apoAI-HDL is assessed by determining the reduction in the internalization and degradation of HDL holoproteins by cell surface receptors.

42.　The method of claim 40 wherein the increase in half life of apoAI-HDL is assessed by determining the reduction in the hepatic and renal clearance of apoAI-HDL holoproteins.

43.　The method of claim 40 wherein the increase in half life of apoAI-HDL is assessed by determining the accumulation of apoAI-HDL.

44.　The method of claim 40 wherein the compound's ability to increase in half life of apoAI-HDL *in vivo* or *in vitro* is assessed by:

　　a)　contacting a hepatic model with the compound and HDL,

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b) determining the level of apoAI-HDL accumulation, and

c) comparing the levels of apoAI-HDL accumulation in a compound-treated hepatic model with a hepatic model not contacted with the test compound.

45. The method of claim 44 wherein the hepatic model comprises HepG2 cells.

46. The method of claim 44 wherein the hepatic model is a cell line stably transfected with the SR-BI gene.

47. The method of claim 44 wherein levels of apoAI-HDL accumulation are determined using an ELISA assay.

48. The method of claim 40 further comprising determining whether the compound causes a concomitant change in apoAI gene expression, a change in apoAI protein synthesis, or a change in plasma LDLc levels.

49. The method of claim 40 wherein the increase in half life of apoAI-HDL is assessed by:

(i) administering the test compound to an animal over an effective time period; and

(ii) monitoring the level of HDLc in the animal.

50. The method of claim 49 further comprising comparing the levels of HDLc in the animal in which the compound was administered with the levels of HDLc in an animal in which the compound was not administered.

51. The method of claim 49 further comprising monitoring the level of serum LDLc in the animal and comparing the levels of LDLc in the animal in which the compound was administered with the levels of LDLc in an animal in which the compound was not administered.

52. The method of claim 49 further comprising assessing the amount of cholesterol/cholesteryl ester present in the bile and/or stool in an animal model, and comparing the amount of cholesterol/cholesteryl ester present in the bile and/or stool as a result of improved reverse cholesterol transport in an animal model in which the compound was administered with the amount of cholesterol/cholesteryl ester present in the bile and/or stool in an animal model in which the compound was not administered.

53. The method of claim 49 wherein the test compound is administered to the animal model for at least six weeks.

54. A method for determining whether a compound improves the functionality of circulating HDL comprising assaying whether the compound causes an increase in the selective uptake of cholesterol or cholesteryl ester.

55. The method of claim 54 wherein the compound is assayed by steps comprising:

    (i)   contacting a cellular hepatic model with a cell surface receptor blocker;

    (ii)   contacting the hepatic model with the compound;

    (iii)   contacting the hepatic model with a labeled HDL laden with cholesteryl ester;

    (iv)   washing the cells from the hepatic model to form washed cells and supernatant; and

    (v)   comparing the amount of label in the washed cells and/or supernatant with the amount of label in control cells and/or supernatant from control cells not treated with a cell surface receptor blocker but treated with the compound.

56. The method of claim 54 wherein the increase in the selective uptake of cholesteryl ester is assayed by measuring cell surface binding of cholesteryl ester laden HDL to hepatic cell

surface receptors.

57. The method of claim 56 wherein the hepatic cell surface receptors are derived from HepG2 cells.

58. The method of claim 56 wherein the hepatic cell surface receptors comprise class B, type I or type II scavenger receptors.

59. The method of claim 56 wherein the cell surface receptors are derived from a cell line stably transfected with the SR-BI gene.

60. The method of claim 55 wherein the cell surface receptor blocker is an antibody against SR-BI/II scavenger receptors.

61. The method of claim 55 wherein the labeled HDL laden with cholesteryl ester contains cholesteryl ether labeled with $^3[H]$.

62. The method of claim 55 wherein the labeled HDL laden with cholesteryl ester contains cholesteryl ether labeled with $^3[H]$ and apoAI-HDL labeled with I^{125}.

63. A method to identify compounds that increase the selective uptake of cholesterol and cholesteryl ester comprising:

    (i) assessing the ability of the compound to form a complex with HDL,

    (ii) assessing the ability of the compound-HDL complex to bind to SR-BI protein, and

    (iii) assessing the ability of the compound to bind to the SR-BI protein

64. A method to assess whether a subject has a variant of apoAI-HDL comprising:

    d) determining whether the subject has a lower than normal response to an HDLc

level elevating drug, and

e) isolating and evaluating the subject's apoAI protein for a genetic variation that result in decreased apoAI–HDL binding to the HDL receptor.

65. The method of claim 41 wherein the reduction in the internalization of HDL holoproteins by cell surface receptors is assessed by measuring the amount of labeled apo-AI-HDL present inside the cell.

66. The method of claim 65 wherein the labeled apoAI-HDL contains apoAI-HDL labeled with I^{125}.

67. The method of claim 41 wherein the reduction in the degradation of HDL holoproteins by cells is assessed by measuring the amount of labeled apoAI-HDL in cell supernatant after acid-mediated precipitation.

68. The method of claim 67 wherein the labeled apoAI-HDL contains apoAI-HDL labeled with I^{125}.

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